

AD 693625

CARDIORESPIRATORY AND METABOLIC RESPONSES TO
LIVE E. COLI AND ENDOTOXIN IN THE MONKEY

C. A. Guenter, V. Fiorica, and L. B. Hinshaw

Technical Report No. 1
University of Oklahoma Medical Center THEMIS Contract

August 11, 1969

Research sponsored by the Office of Naval Research
Contract N00014-68-A-0496
Project NR 105-516

Reproduction in whole or in part is permitted for
any purpose of the United States Government

This document has been approved for public release
and sale; its distribution is unlimited.

MEDICAL CENTER RESEARCH AND DEVELOPMENT OFFICE
OF THE UNIVERSITY OF OKLAHOMA FOUNDATION, INC.

ACKNOWLEDGMENTS

We express appreciation to Miss Jan Seamans, Mrs. Geraldine Imundo, and Mrs. Martha Mathis for valuable technical assistance.

TABLE OF CONTENTS

	Page
ABSTRACT	1
INTRODUCTION	1
METHODS	2
RESULTS	4
DISCUSSION	9
REFERENCES	12

ABSTRACT

Septicemia and the administration of endotoxin may have different effects in the production of shock. Hemodynamic, respiratory, and metabolic effects of live organisms (Escherichia coli) were compared with endotoxin and saline in rhesus monkeys. Six animals were given E. coli, six endotoxin, and five served as controls. Studies were conducted for 2-4 hours. The mean cardiac output decreased 62% within 60-90 minutes in the E. coli group and 41% in the endotoxin group. This was associated with a dramatic decrease in systemic pressure and peripheral resistance in all animals. The mean arterial P_{CO_2} decreased to 24 mm Hg in the E. coli group and 26 mm Hg in the endotoxin group. Arterial hypoxemia developed in four animals and high alveolo-arterial oxygen gradients were present at some time during the study in all the animals. Blood lactate levels increased and catecholamine levels rose after 1-2 hours of hypotension. Control animals did not demonstrate these changes. The profound hemodynamic, respiratory, and metabolic effects of the septicemia in the monkey simulate observations in humans in septic shock. The rate of onset of measurable changes and the severity of hypoxia were the major differences observed in E. coli and endotoxin groups.

INTRODUCTION

Patients with septic shock present a wide spectrum of hemodynamic and metabolic derangements (3, 8, 13, 14, 17, 21, 23). The difficulty of detailed, sequential studies in the human under controlled conditions makes exploration of the pathophysiology and treatment of septic shock in the animal model essential. Much of the data available is concerned with endotoxin and the nonprimate animal model. Species differences in

hemodynamic response to endotoxin have been emphasized (9, 16, 22) and the canine endotoxin model challenged in particular (22). Recent studies using the primate animal model for vascular research (6, 9, 11, 15, 16) document normal hemodynamic characteristics and the feasibility of using the primate as a shock model. Although profound hemodynamic changes can be produced in the primate by the injection of endotoxin (9, 11, 15, 16), there is reason to believe that septicemia may have effects not necessarily reproduced by endotoxin injection (3, 10, 22). Thus the subhuman primate with septic shock may have advantages as an animal model.

In this study we have explored the effects of infusion of live organisms (Escherichia coli), as compared to endotoxin and saline, in three groups of anesthetized rhesus monkeys. Hemodynamic, respiratory, and metabolic parameters were monitored. Serum catecholamine and blood lactate levels were determined in several animals in each group.

METHODS

Seventeen healthy adult monkeys (rhesus macaque) were selected for this study. The animals were captured in the wild and utilized after appropriate inspection to exclude transmissible disease. All were in apparent good health. The physical characteristics are listed in Table 1.

In each instance, the animal was given 20-30 mg/kg pentobarbital intravenously. Supplemental intravenous pentobarbital was given when the animal showed evidence of rousing. The animal was placed in the supine position, and a cutdown performed to isolate the femoral artery and vein. A No. 6 NIH woven nylon catheter was advanced to the right atrium under fluoroscopic control and a Teflon needle introduced into the

femoral artery. A cuffed endotracheal tube was introduced into the upper trachea and the cuff inflated to permit collection of expired gases. The endotracheal tube was connected to a breathing valve with an 8-ml dead space, and expired gases were collected in a water-sealed spirometer during at least a 2-minute period. Simultaneous determinations of arterial P_{CO_2} , P_{O_2} , and pH were performed.

The expired gases and arterial blood were analyzed on an Instrumentation Laboratories blood gas analyzer and pH electrode. Minute ventilation, tidal volume, oxygen consumption, carbon dioxide production, respiratory exchange ratio, physiological dead space, and alveolar P_{O_2} were calculated using this data (2). Alveolar P_{CO_2} was assumed equal to arterial P_{CO_2} .

The cardiac output was measured during the expired gas collection by the indicator-dilution technique. Indocyanine green (1.0 mg) was injected into the right atrium or pulmonary artery with sampling from the femoral artery. The blood was withdrawn by a Harvard infusion pump at the rate of 23 ml/min through a densitometer cuvette (Gilford Instrument Laboratories, Inc.) and the blood was reinfused. The volume withdrawn during each dye curve was less than 20 ml and was associated with a mean systemic pressure drop of less than 10 mm Hg. The area under the curves was determined by the semilogarithmic plotting technique. At least duplicate determinations were made in each instance. Pressures were recorded from catheters in the right atrium and femoral artery by means of Statham P23Db pressure transducers. A Sanborn 350 series ultraviolet photographic recorder was employed.

The temperature was monitored by a thermistor rectal probe and the spontaneous decrease in temperature during anesthesia was prevented by means of a warming blanket.

Hematocrit determinations were made at the time blood gas analyses were performed throughout the study. Blood lactate levels were determined by the method of Barker and Summerson (1). Plasma catecholamine levels were determined as previously described (4). Base-line hemodynamic, ventilatory, and arterial blood analyses were performed and, in several instances, blood lactate and catecholamine levels were determined. Five animals were then given injections of saline, six animals were given 4 mg/kg of E. coli endotoxin (Difco), and six were given $4-6 \times 10^9$ organisms/kg of live E. coli, prepared as previously described (10). The endotoxin and E. coli were injected over a 3- to 15-minute period. All injections were made into the right atrium with the exception of one endotoxin injection which was made into the descending aorta. Studies were repeated at frequent intervals over at least a 3-hour period in all animals except those which expired early in the study.

Statistical analysis was performed by the "t" test, comparing endotoxin and E. coli groups with the control group.

RESULTS

The control animals were stable throughout the period of study. Dramatic changes were noted in most parameters measured in both the endotoxin and E. coli groups. One animal given endotoxin died 2.5 hours after the infusion. Three animals given E. coli died within 3.5 hours of the time of infusion. Those animals which survived the study period were sacrificed after 4 hours.

Hemodynamic characteristics. The mean initial cardiac output was 0.14 liter/kg per minute (SD 0.05) in the 17 animals. The percentage change in cardiac output during

the study in each group of animals is plotted in Figure 1. In the control animals, the mean cardiac output was 0.14 liter/kg per minute with no consistent change throughout the study period. The animals given endotoxin had a mean initial cardiac output of 0.13 liter/kg per minute, which decreased early after the injection of endotoxin and progressively decreased in most instances. Animals given E. coli had a mean cardiac output of 0.14 liter/kg per minute during the initial observation and developed a gradual progressive decrease throughout the study. This decrease in cardiac output in E. coli and endotoxin groups was significant ($P < .01$) at all times more than 90 minutes after infusion.

The mean systemic arterial pressure was 102 mm Hg (SD 28) during the initial period in the 17 animals. The mean pressure was 105 mm Hg for the control animals and gradually rose to 113 mm Hg at the end of the study. The mean pressure was 111 mm Hg for the endotoxin-treated animals, decreased to 35 mm Hg within 90 minutes of the infusion, and then rose to 64 mm Hg by the end of the study. The mean pressure was 89 mm Hg for the E. coli-treated animals, decreased to 28 mm Hg within 90 minutes, and then rose to 40 mm Hg by the end of the study. This decrease in systemic pressure in the E. coli and endotoxin groups was significant ($P < .01$). The relationship of the cardiac output to arterial pressure is reflected in the early decrease in systemic resistance, with a late rise in resistance as illustrated in Figure 2.

The mean initial systemic resistance was $9,800 \text{ dynes-sec cm}^{-5}$ in the 17 animals. The percent changes in systemic resistance are plotted in Figure 2. Control animals had a mean initial resistance of $11,200 \text{ dynes-sec cm}^{-5}$ and this increased minimally in most animals. The endotoxin group had an initial resistance of $10,000 \text{ dynes-sec cm}^{-5}$,

with a dramatic early drop in resistance ($P < .05$) followed by a late rise toward control levels and in some instances exceeding control levels. The E. coli group had an initial resistance of $8,000 \text{ dynes-sec cm}^{-5}$, an early decrease in resistance ($P < .05$) followed by a late increase in systemic resistance.

The mean initial heart rate was 208 beats/min in the 17 animals with a mean value of 198 for the control group, 209 for the endotoxin group, and 217 for the E. coli group. Heart rates are plotted for the entire study in Figure 3. Although heart rates generally increased in the control animals, these increases were more striking in the endotoxin group. The E. coli group had a greater variability in heart rates and one animal developed a marked bradycardia just prior to death. Heart rates in these groups were not statistically different.

The mean initial right atrial pressure was 1.8 mm Hg in 11 animals. Mean right atrial pressure varied less than ± 2 mm Hg throughout the study in control animals. The endotoxin and E. coli groups had a decrease in right atrial pressure of 1-2 mm Hg during the most profound hypotension, and these pressures never exceeded control values by more than 1 mm Hg.

Ventilatory characteristics. The mean initial minute ventilation was 0.27 liter/kg (SD 0.13) in the 17 animals. Figure 4 demonstrates the variation in minute ventilation in the three groups. Although control animals generally increased their ventilation during the study, more marked changes were seen in the endotoxin and E. coli groups. All three of the animals, whose minute ventilation decreased, died during the study. The mean initial oxygen consumption was 5.7 ml/kg (SD 2.1) in the 17 animals. Although the values were relatively stable throughout the study in control animals, they varied

widely and inconsistently in the endotoxin and E. coli groups. Several of these animals had profound decreases in oxygen consumption.

Blood gas exchange. The arterial PO_2 values for the three groups are plotted in Figure 5. The mean initial arterial PO_2 was 80 mm Hg (SD 8.0) in the 17 animals. The PO_2 remained unchanged or increased during the study in control animals, but demonstrated a sharp decrease immediately after infusion of endotoxin with a gradual return toward normal levels. Although several animals given E. coli developed hypoxia, this did not occur as predictably or as early as with endotoxin. In general, the alveoloarterial (A-a) oxygen tension gradients were maintained near initial values in the control animals. Only one control animal had an A-a gradient greater than 28 mm Hg at any time during the study. In the E. coli and endotoxin groups all animals had A-a gradients greater than 30 mm Hg at some time during the study.

The arterial P_{CO_2} values are plotted in Figure 6. As is apparent, the control animals hyperventilated somewhat as the study progressed, but the decrease in P_{CO_2} was more dramatic ($P < 0.05$) in the animals given endotoxin or E. coli. This decrease in P_{CO_2} was related to development of a metabolic acidosis. Although most animals maintained a pH greater than 7.38 (Figure 7), several animals in the E. coli and endotoxin groups demonstrated acidosis which was not entirely compensated by hyperventilation. The one animal that developed CO_2 retention (P_{CO_2} 65 mm Hg) died during the study.

The physiological dead space in the monkeys was similar in all three groups during the initial resting studies. The dead space was relatively constant in the control group throughout the study. As is apparent in Figure 8, the dead space increased in many of the animals in the E. coli and endotoxin groups, suggesting that ventilation perfusion relationships were altered.

The mean initial hematocrit was 38% in the control, 36% in the endotoxin, and 38% in the E. coli groups. During the course of the studies these groups demonstrated a mean decrease in hematocrit of 5.4, 2.5, and 5.6%, respectively. These differences are not statistically significant. This was associated with the removal of 20-30 ml of blood and infusion of 30-60 ml of saline, endotoxin, or E. coli solutions.

Blood lactate levels ranged from 11 to 17 mg/100 ml in the initial base-line period. After 2 hours of hypotension, the lactates ranged from 27 to 105 mg/100 ml in the three animals tested.

The plasma catecholamines and systemic resistance are plotted in Table 2. The catecholamines ranged from 0.67 to 1.98 µg/liter in two animals given saline only. No consistent change was noted during the 4-hour study period. Four animals given E. coli had catecholamine levels of 1.04-2.14 µg/liter during the initial period. One to two hours after infusion of E. coli the values ranged from 0.98 to 2.38 µg/liter but during the second to fourth hours they ranged from 3.00 to 26.27 µg/liter. Thus there was a delayed increase in the serum catecholamine levels. Four animals in the endotoxin group had catecholamine levels ranging from 0.94 to 2.70 µg/liter during the initial period. Within the first hour these were elevated in two animals. Two to four hours after infusion of endotoxin the values ranged from 2.47 to 13.24 µg/liter and were highest in the animal that died (No. 9). As is apparent in Table 2, the systemic resistance was uniformly decreased in the E. coli and endotoxin groups during the period 1-2 hours after injection. Only animals 9 and 10 had elevated catecholamine levels at this time. All the animals in these groups had an increase in systemic resistance (when compared to the 1- to 2-hour period) later in the study. These were associated with increased catecholamine levels in all animals except No. 10.

DISCUSSION

The base-line data in these studies and the hemodynamic effects of infusion of endotoxin compare favorably with those reported in the unanesthetized monkey (16). This suggests that the anesthetic does not obscure major cardiovascular responses.

The demonstration of profound hemodynamic and metabolic effects of infusion of live E. coli is not surprising in view of the data previously reported in dogs (10). The most striking difference between the group given endotoxin and E. coli was the time of onset of measurable changes. Animals given endotoxin developed hypotension, decreased cardiac output, and ventilatory changes much earlier than those given E. coli. The severe hypoxia observed within 5 minutes of infusion of endotoxin was not observed in any of the animals given E. coli; however, all animals in these two groups demonstrated decreased arterial P_{O_2} or increased A-a gradients at some time during the course of the study.

The profound hypotension observed in both the E. coli and endotoxin groups was apparently related to a rapidly decreasing cardiac output and a decrease in peripheral resistance. This pattern was previously reported in monkeys given endotoxin (9, 16). The gradual increase in peripheral resistance after approximately 2 hours was also observed by Nies et al. (16) who suggested that the dramatic early decrease in peripheral resistance was a result of circulating kinins.

The mechanism of decreased cardiac output after infusion of endotoxin or E. coli is not established. The administration of volume expanders has generally resulted in an increase in cardiac output in patients with septic shock (3, 8, 13, 14, 17) suggesting that myocardial contractility is not the limiting factor. Studies in the dog (5) indicated that myocardial contractility is not an important problem during the first three hours of endotoxin shock. On the other hand, cats demonstrated sharp reductions in stroke volume and mean ejection

rate for a given left ventricular end-diastolic pressure, after endotoxin infusion (19). Electron microscopy did not demonstrate mitochondrial changes in the rhesus monkey myocardium during the 4-hour period after infusion of endotoxin (15). Furthermore, it has been demonstrated that after infusion of endotoxin, the venous return is decreased in association with the profound drop in cardiac output (9). Since the right atrial pressure was never elevated in the animals in our study, it is unlikely that myocardial failure was a primary event in producing the decreased cardiac output. Thus, the profound changes in cardiac output may result entirely from decreased peripheral resistance and venous return.

The pulmonary effects of endotoxin are well recognized in the animal (7, 13, 20). They include decreased compliance of the lungs, increased airway resistance, and increased pulmonary artery, capillary, and pulmonary vein pressure (without elevations of left atrial pressure). Hypoxia has been attributed to altered ventilation perfusion ratios. This series of animals demonstrates the hyperventilation, hypoxia, and increased A-a gradients described in patients with septic shock. The precise mechanism of pulmonary changes has not been established. Simmons et al. (18) have demonstrated hyperventilation and hemodynamic changes following intracisternal injections of endotoxin in dogs. The role of the central nervous system in the ventilatory response in the primate has not been explored.

Blood lactate levels rose in animals given E. coli or endotoxin but there was no correlation between the degree of rise and the severity of the hypotension. The magnitude of rise was generally less than has been reported in shock in patients (8, 13). This increase in blood lactate is at least partly responsible for the metabolic acidosis.

Plasma catecholamine levels were in general minimally elevated until the second hour of hypotension and then rose modestly. This rise of catecholamines was not noted in a previous report (11) because of the short duration of the study. The precise nature of the catecholamines was not defined. It is possible that the late rise in peripheral resistance seen in most animals was related to the increase in catecholamine levels.

These studies following infusion of live organisms (E. coli) indicate that the rhesus monkey develops hemodynamic, ventilatory, blood gas exchange, and metabolic alterations similar to the human in septic shock. It is likely that pathophysiological and therapeutic studies in such a model will have more reliable implications for the treatment of patients with this syndrome.

REFERENCES

1. Barker, S. B., and W. H. Summerson. The colorimetric determination of lactic acid in biological material. J. Biol. Chem. 138: 535-554, 1941.
2. Comroe, J. H., R. E. Forster, A. B. DuBois, W. A. Briscoe, and E. Carlsen. The Lung. Chicago: Year Book, 1962, p. 323.
3. Dietzman, R. H., J. H. Block, J. A. Feemster, Y. Idzuke, and R. C. Lillehei. Mechanisms in the production of shock. Surgery 62: 645-654, 1967.
4. Fiorica, V. An improved semiautomated procedure for fluorometric determination of plasma catecholamines. Clin. Chim. Acta 12: 191-197, 1965.
5. Goodyer, A. V. N. Left ventricular function and tissue hypoxia in irreversible hemorrhagic and endotoxin shock. Am. J. Physiol. 212: 444-450, 1967.
6. Guenter, C. A., D. R. McCaffree, L. J. Davis, and V. S. Smith. Hemodynamic characteristics and blood gas exchange in the baboon. J. Appl. Physiol. 25: 507-510, 1968.
7. Halmagyi, D. F. J., B. Starzecki, and G. J. Horner. Mechanisms and pharmacology of endotoxin shock in sheep. J. Appl. Physiol. 18: 544-552, 1963.
8. Hardaway, R. M., P. M. James, Jr., R. W. Anderson, C. E. Bredenberg, and R. L. West. Intensive study and treatment of shock in man. J.A.M.A. 199: 779-790, 1967.
9. Hinshaw, L. B., T. E. Emerson, and D. A. Reins. Cardiovascular responses of the primate in endotoxin shock. Am. J. Physiol. 210: 335-340, 1966.
10. Hinshaw, L. B., L. A. Solomon, D. D. Holmes, and L. J. Greenfield. Comparison of canine responses to E. coli organisms and endotoxin. Surg. Gynec. Obstet. 127: 981-988, 1968.

11. Hinshaw, L. B., L. A. Solomon, D. A. Reins, and V. Fiorica. Sympathoadrenal system and renal response to endotoxin in the primate. Nephron. 4: 394-404, 1967.
12. Kuida, H., L. B. Hinshaw, R. P. Gilbert, and M. B. Visscher. Effect of gram-negative endotoxin on pulmonary circulation. Am. J. Physiol. 192: 335-344, 1958.
13. MacLean, L. D., W. G. Mulligan, A. P. H. McLean and J. H. Duff. Patterns of septic shock in man--a detailed study of 56 patients. Ann. Surg. 166: 543-562, 1967.
14. MacLean, L. D., W. G. Mulligan, A. P. H. McLean and J. H. Duff. Alkalosis in septic shock. Surgery 655-662, 1967.
15. McKay, D. G., W. Margarethen, and I. Csavassy. An electron microscope study of endotoxin shock in rhesus monkeys. Surg. Gynec. Obstet. 125: 825-832, 1967.
16. Nies, A. S., R. P. Forsyth, H. E. Williams, and K. L. Melmon. Contribution of kinins to endotoxin shock in unanesthetized rhesus monkeys. Circ. Res. 22: 155-164, 1968.
17. Siegel, J. H., M. Greenspan, and L. R. M. Del Guercia. Abnormal vascular tone, defective oxygen transport and myocardial failure in human septic shock. Ann. Surg. 165: 504-517, 1967.
18. Simmons, R. L., R. W. Anderson, T. B. Ducker, H. K. Sleeman, J. A. Collins, and K. P. Boothman. The role of the central nervous system in septic shock. II. Hemodynamic, respiratory and metabolic effects of intracisternal and intraventricular endotoxin. Ann. Surg. 167: 158-167, 1968.
19. Solis, R. T. and S. E. Downing. Effects of E. coli endotoxemia on ventricular performance. Am. J. Physiol. 211: 307-313, 1966.

20. Stein, M., and D. P. Thomas. Role of platelets in the acute pulmonary responses to endotoxin. J. Appl. Physiol. 23: 47-52, 1967.
21. Strauch, M., J. S. McLaughlin, A. Mansberger, J. Young, P. Mendonca, K. Gray, and R. A. Cowley. Effects of septic shock on renal functions in humans. Ann. Surg. 165: 536-543, 1967.
22. Waisbren, B. A. Gram-negative shock and endotoxin shock. Am. J. Med. 36: 819-824, 1964.
23. Wilson, R. G., A. D. Chiscano, E. Quadros, and M. Tower. Some observations in 132 patients with septic shock. Anesthesia Analgesia 46: 751-763, 1967.

TABLE 1
Physical Characteristics of Animals

	Animal No.	Weight (kg.)	Sex
Control	1	5.5	F
	2	5.5	M
	3	6.0	M
	4	5.6	M
	5	6.2	M
Endotoxin	6	5.7	M
	7	9.8	M
	8	9.1	M
	9	4.2	F
	10	9.8	M
	11	6.0	F
<u>E. coli</u>	12	5.6	M
	13	7.6	F
	14	6.0	F
	15	6.2	M
	16	5.7	F
	17	7.8	F

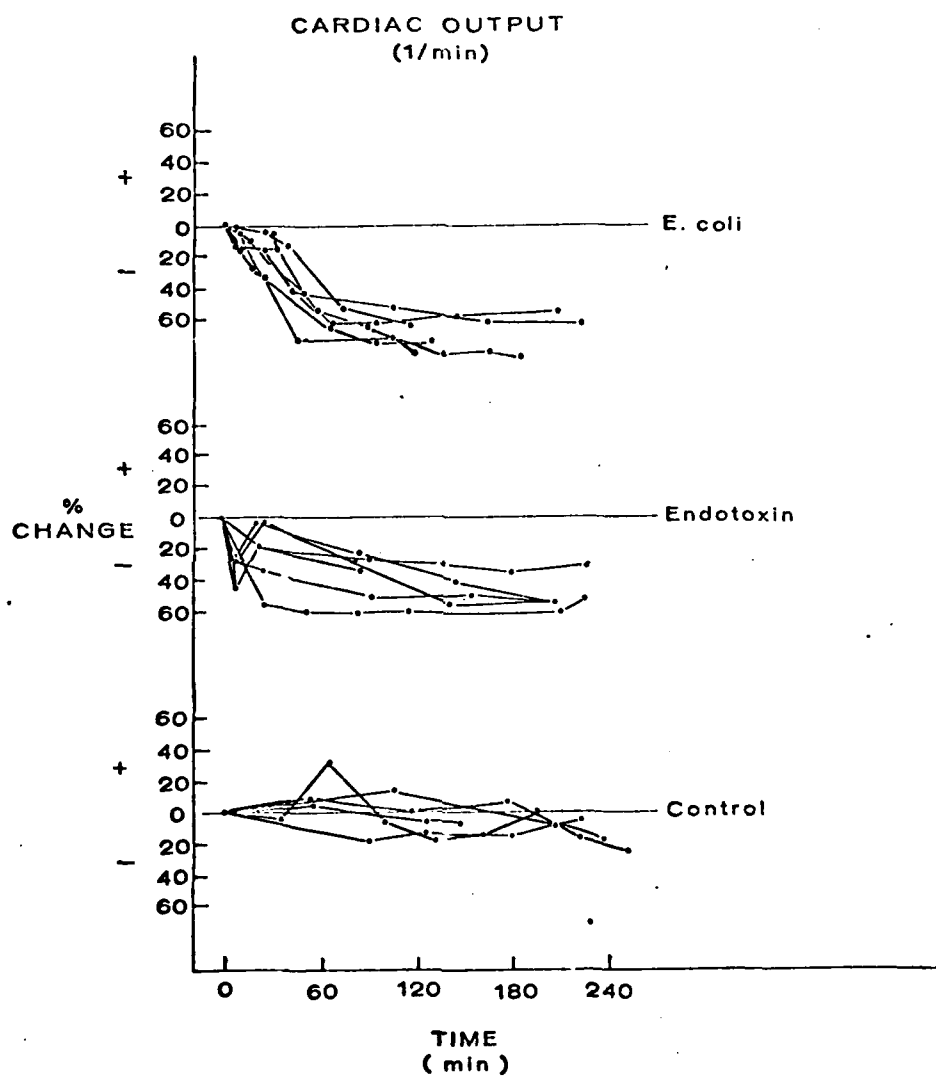


Figure 1

Percentage change in cardiac output in *E. coli*, endotoxin and control animals. Baseline measurements at 0 time were prior to the injections of these agents.

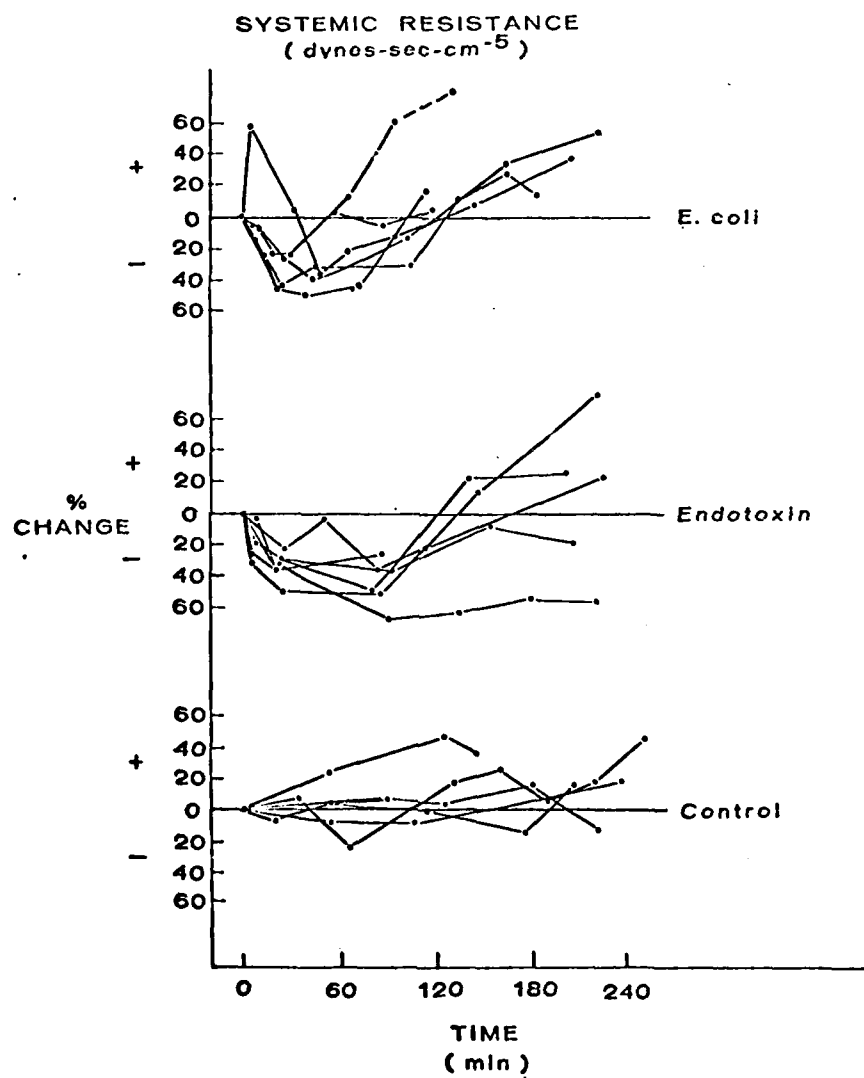


Figure 2

Percent change in systemic resistance in E. coli, endotoxin and control animals.

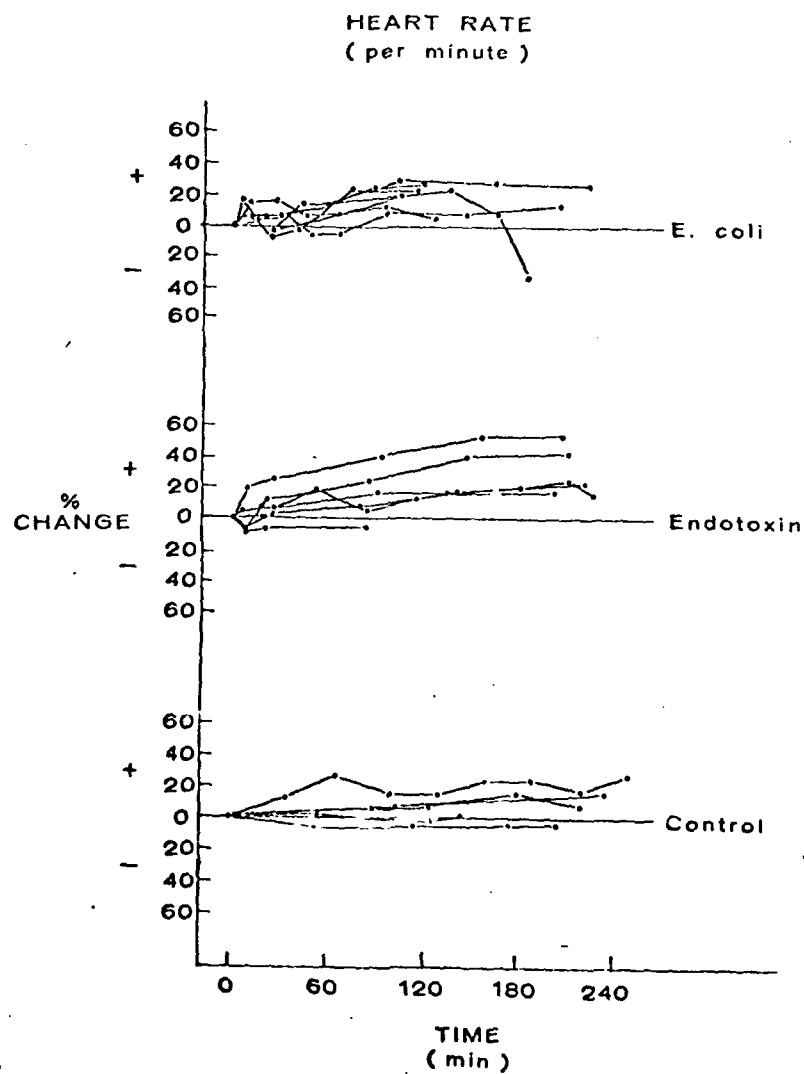


Figure 3

Percent change in heart rate in E. coli, endotoxin, and control animals.

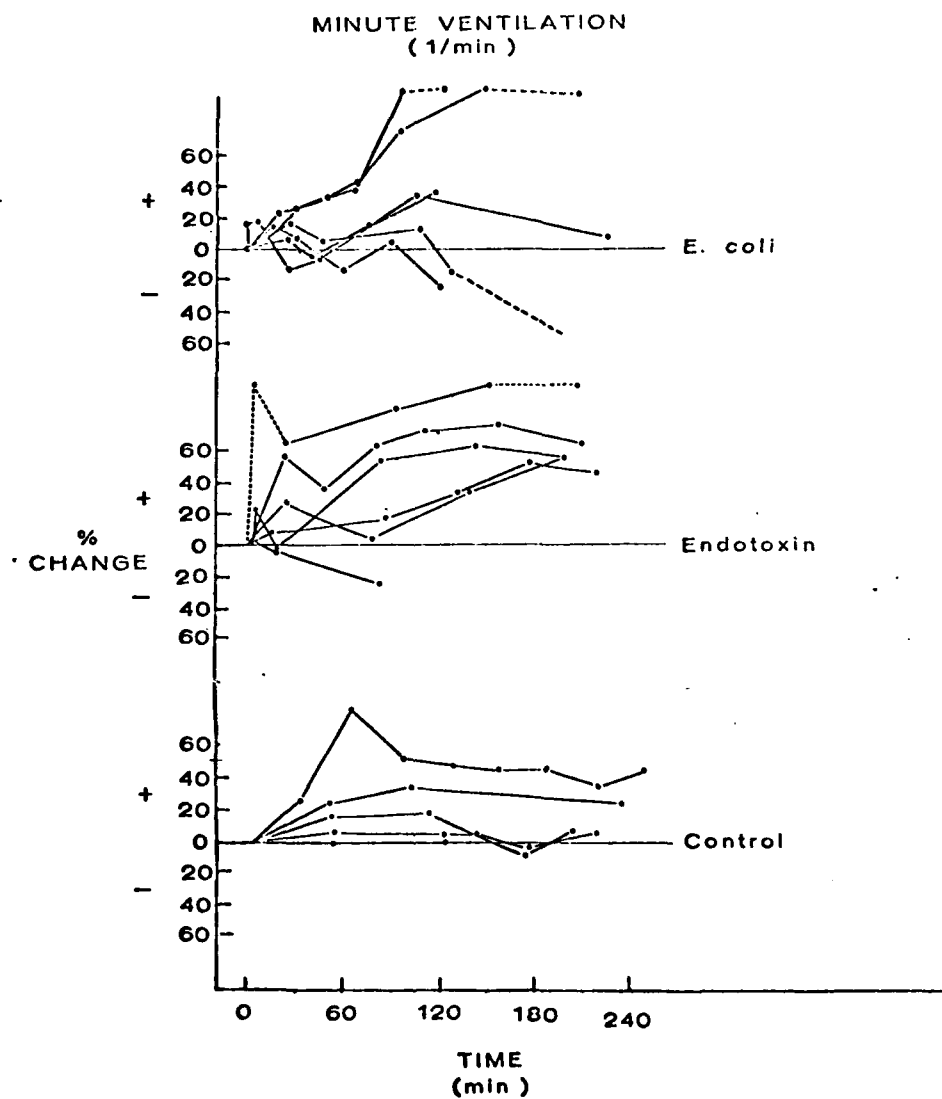


Figure 4

Percent change in minute ventilation in *E. coli*, endotoxin, and control animals. Points joined by dotted lines are off scale.

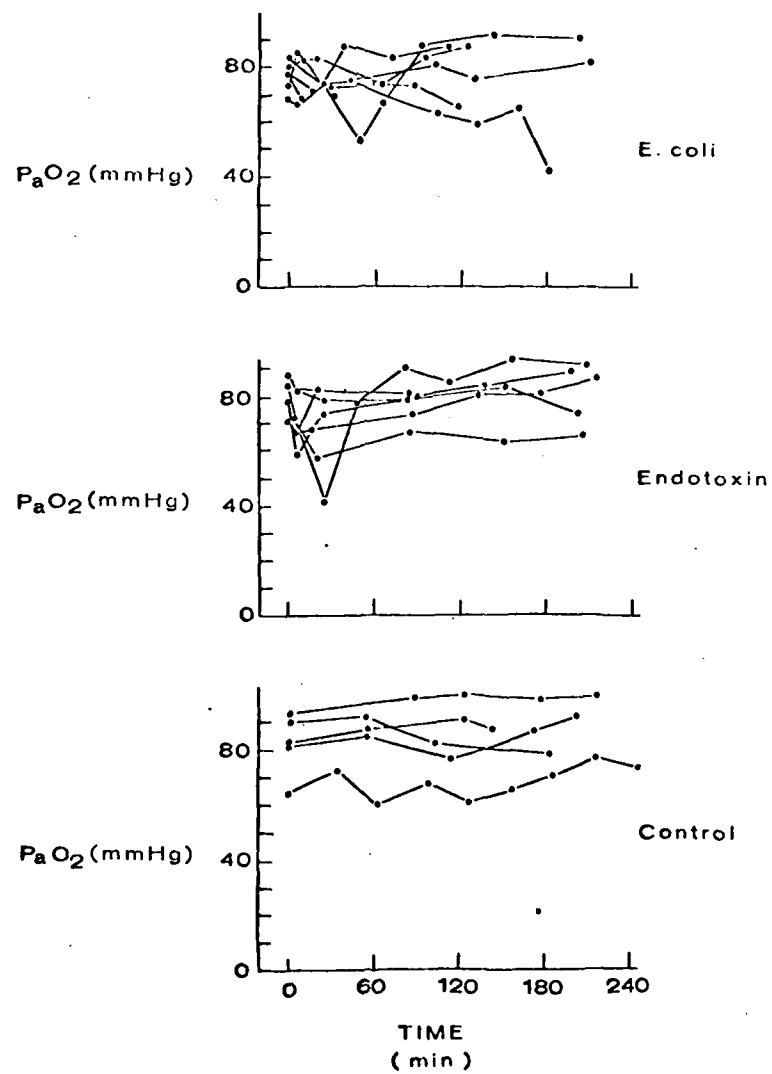


Figure 5

Arterial P_{O_2} in E. coli, endotoxin, and control animals.

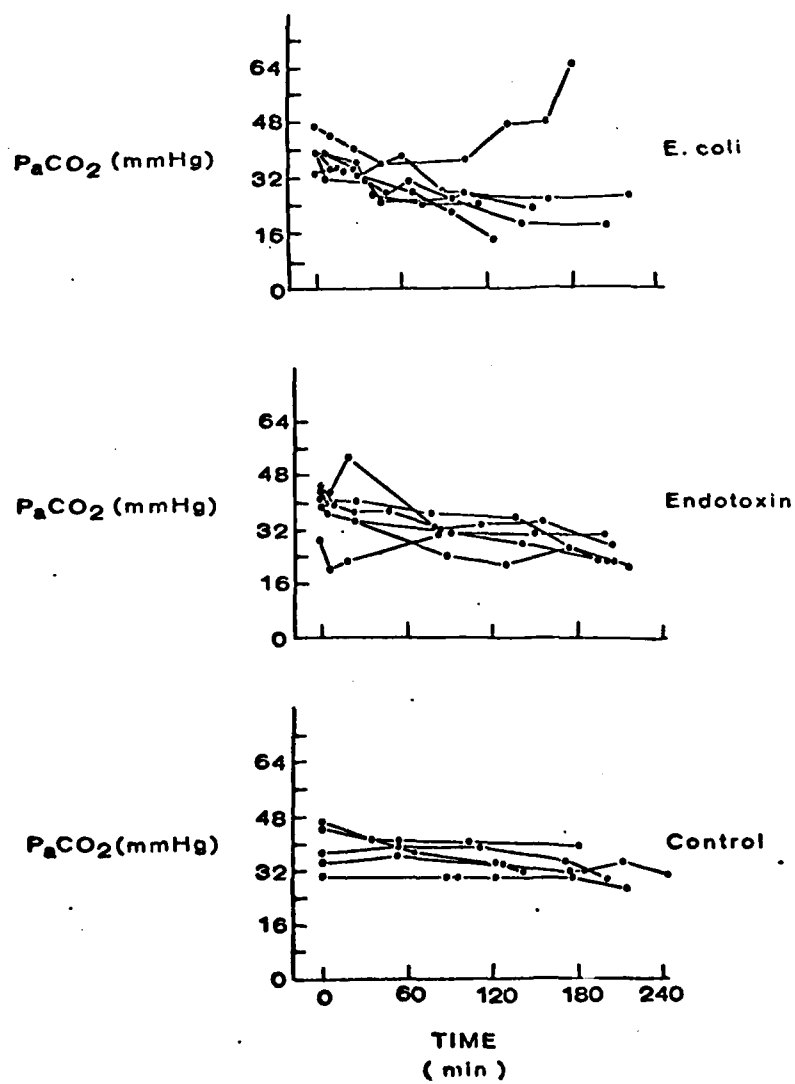


Figure 6

Arterial P_{CO_2} in E. coli, endotoxin, and control animals.

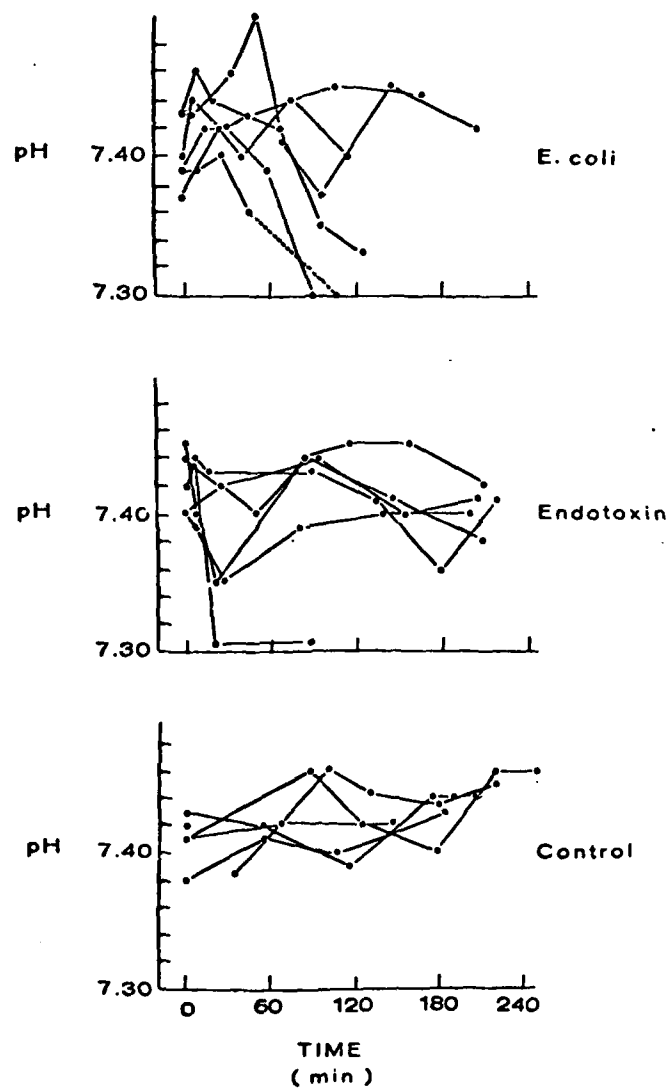


Figure 7

Arterial pH in E. coli, endotoxin, and control animals.

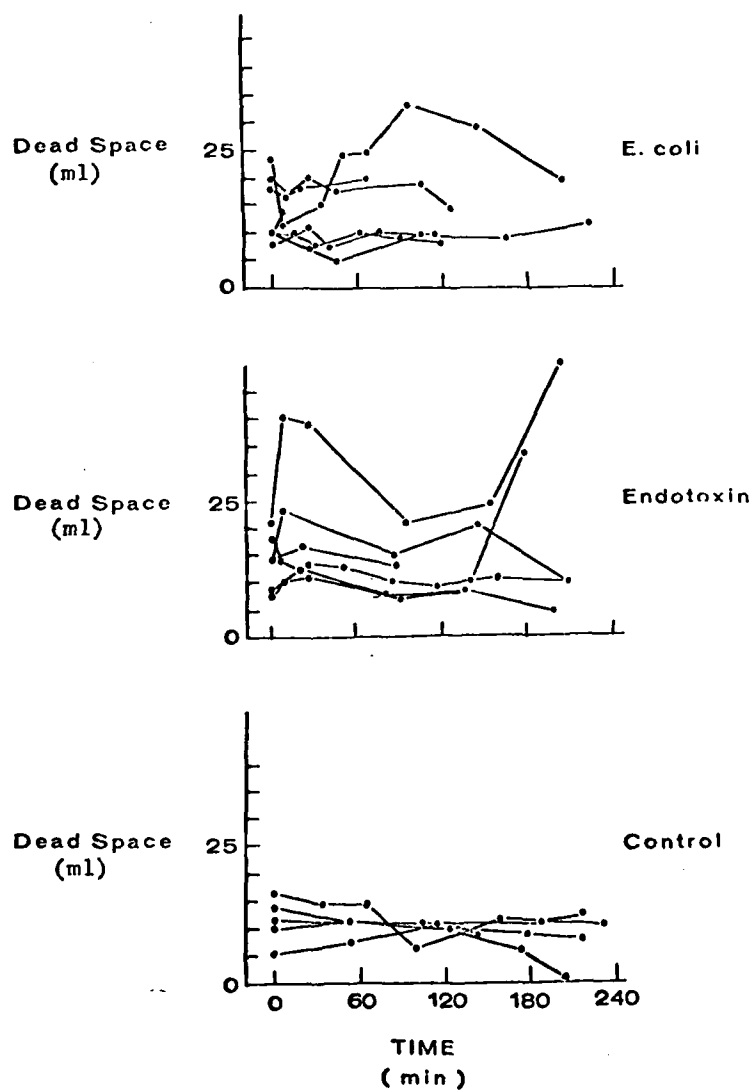


Figure 8

Physiological dead space (ml) in E. coli, endotoxin and control animals.

TABLE 2
Relationship of Serum Catecholamine Levels to Systemic Resistance

	Animal No.		Baseline	1-2 hr	2-4 hr
Control	3	C	0.67	0.67	0.79
		SR	7,000	7,000	8,000
	4	C	1.67	1.88	1.98
		SR	7,000	9,300	10,500
<u>E. coli</u>	12	C	1.34	1.14	16.0
		SR	9,500	6,600	10,900
	13	C	1.80	1.67	10.17
		SR	4,900	4,600	6,800
	14	C	2.14	2.38	26.27
		SR	9,300	7,000	13,300
	15	C	1.04	0.98	3.00
		SR	7,300	5,500	11,300
Endotoxin	7	C	0.94	1.18	2.47
		SR	7,000	4,300	5,700
	8	C	1.21	1.26	3.80
		SR	11,900	3,700	4,900
	9	C	2.70	11.70	13.24
		SR	12,500	9,200	-
	10	C	1.26	9.12	3.28
		SR	10,800	5,400	13,300

Baseline measurements were made prior to injection of E. coli or endotoxin, subsequent measurements at 1-2 or 2-4 hours after injection. C = catecholamine levels in $\mu\text{g/liter}$; SR = systemic resistance in dynes-sec cm^{-5} .

Unclassified

Security Classification

DOCUMENT CONTROL DATA - R & D		
<i>(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)</i>		
1. ORIGINATING ACTIVITY (Corporate author)		2a. REPORT SECURITY CLASSIFICATION
Medical Center Research and Development Office of the University of Oklahoma Foundation, Inc.		Unclassified
		2b. GROUP
		Unclassified
3. REPORT TITLE		
Cardiorespiratory and Metabolic Responses to live <u>E. coli</u> and Endotoxin in the Monkey		
4. DESCRIPTIVE NOTES (Type of report and, inclusive dates)		
Technical Report		
5. AUTHOR(S) (First name, middle initial, last name)		
C. A. Guenter, V. Fiorica, and L. B. Hinshaw		
6. REPORT DATE	7a. TOTAL NO. OF PAGES	7b. NO. OF REFS
August 11, 1969	24	23
8a. CONTRACT OR GRANT NO.	9a. ORIGINATOR'S REPORT NUMBER(S)	
N00014-68-A-0496	1	
b. PROJECT NO.		
NR 105-516		
c.	9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)	
d.		
10. DISTRIBUTION STATEMENT		
This document has been approved for public release and sale; its distribution is unlimited.		
11. SUPPLEMENTARY NOTES		12. SPONSORING MILITARY ACTIVITY
		Office of Naval Research
13. ABSTRACT		
<p>Septicemia and the administration of endotoxin may have different effects in the production of shock. Hemodynamic, respiratory, and metabolic effects of live organisms (<u>Escherichia coli</u>) were compared with endotoxin and saline in rhesus monkeys. Six animals were given <u>E. coli</u>, six endotoxin, and five served as controls. Studies were conducted for 2-4 hours. The mean cardiac output decreased 62% within 60-90 minutes in the <u>E. coli</u> group and 41% in the endotoxin group. This was associated with a dramatic decrease in systemic pressure and peripheral resistance in all animals. The mean arterial P_{CO_2} decreased to 24 mm Hg in the <u>E. coli</u> group and 26 mm Hg in the endotoxin group. Arterial hypoxemia developed in four animals and high alveolo-arterial oxygen gradients were present at some time during the study in all the animals. Blood lactate levels increased and catecholamine levels rose after 1-2 hours of hypotension. Control animals did not demonstrate these changes. The profound hemodynamic, respiratory, and metabolic effects of the septicemia in the monkey simulate observations in humans in septic shock. The rate of onset of measurable changes and the severity of hypoxia were the major differences observed in <u>E. coli</u> and endotoxin groups.</p>		

DD FORM 1473 (PAGE 1)
1 NOV 65
S/N 0101-807-6811

Unclassified

Security Classification

A-3140x